UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/369,992	08/06/1999	ANNA KATE URSULA KARA	64-99	7524

23713 7590 05/09/2005

GREENLEE WINNER AND SULLIVAN P C
4875 PEARL EAST CIRCLE
SUITE 200
BOULDER, CO 80301

EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 05/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/369,992	KARA ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-58 have been canceled; new claims 59-71 have been added.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn

3. All prior claims have been canceled and all new claims submitted. All prior objections and rejections are withdrawn over canceled claims. Applicant's Amendment has necessitated new grounds of rejection.

Response To Arguments

4. Applicant's arguments filed February 14, 2005 have been fully considered but they are not persuasive.

5. Gardner et al (1993) is traversed on the grounds that Gardner et al does not discuss a biological sample from a human or animal.

6. It is the position of the examiner that Gardner et al (1993) utilized an erythrocyte infected cell sample (see page 1068, col. 1, last paragraph).

7. Gardner et al (1993) is further traversed that the reference does not disclose "the particular sequence (nucleotides 1147-1740 or a 15 consecutive nucleotide probe or primer derived in sequence therefrom)".

8. It is the position of the examiner that Applicant's traversal is not commensurate in scope with what is now claimed. New claim 59 recites open language "comprising" on line 3 of the claim, and the phrase "15 or more consecutive nucleotides thereof". The nucleic acid reagent of

Gardner et al comprised 171 consecutive nucleic acids of the recited range of SEQ ID NO 1, and therefore meets the recited claim limitations. While the introductory phrase "probe or primer consists of" is set forth in claim 59, this phrase defines the minimum number of nucleotides in the probe or primer, and the "contacting" methods steps comprises this probe or primer. The term "consists of" in a claim that recites "comprising" is not the controlling operator for whether the claim may permit the presence or absence of additional components or in this case additional nucleotides. Gardner et al disclose a probe or primer that consists of 171 consecutive nucleic acids of SEQ ID NO 1 within the range of 1147-1740, and comprises additional nucleotides, wherein the probe or primer successfully detected a human Plasmodium malarial agent in a biological sample.

9. Applicant traverses the Obst et al reference for not teaching the sequence relatedness for other species of Plasmodium.

10. It is the position of the examiner that Obst et al was cited for what it taught with respect to analogous art with respect to types of biological samples that are readily incorporated into methods of detecting malarial agents of humans, specifically dried blood samples and for what the reference taught with respect to the utilization of a non-isotopic reporter molecule biotin in methods of detecting a signal in a hybridization assay. Clearly Obst et al provided guidance, suggest and teaching for the utilization of dried blood samples (see page 101, col. 2, "Bloodsmears were obtained" and "were air-dried") and a non-isotopic reporter molecule biotin (see page 101, col. 1, "sensitive in situ hybridization"; and col. 2, "successfully used for the immunocytochemical detection of in situ hybridized biotinylated probes" of Plasmodium; see page 102, col. 2, paragraph 2 "The data clearly show that only the biotinylated malarial probes

resulted in a specific signal with high resolution over P. berghei nuclei") for malarial agents (see page 101, col. 1, paragraphs 1-2).

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 59-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 59 and dependent claims 60-71 recite the phrase "the nucleic acid or sample". While each term in the phrase evidences antecedent basis in claim 59, the term "nucleic acid" is used to describe both the "nucleic acid probe or primer" and "a nucleic acid sample". Clarification of which of the occurrences the phrase refers would provide for clarity of the claim. Amendment of this cited phrase to recite "the nucleic acid"----from said biological sample--- could obviate this rejection.

Claim Rejections - 35 USC § 102

13. Claims 59-64, 66-69 are rejected under 35 U.S.C. 102(b) as being anticipated by Gardner et al (1993, reference of record) in light of Gardner et al (1991, MBP pages 115-124 (b) and 1991, MBP pages 77-88 (a)) references incorporated by reference in Gardner et al 1993)..

14. Gardner et al disclose the instantly claimed invention directed to a method of detecting the presence or absence of a malarial agent in a biological sample, the method comprising the steps of:

Instant claims 59, 64, and 66-67 :

15. **(a) Providing** a biological sample (see page 1068 "erythrocytes", col. 1, last paragraph),

16. **(b) Contacting** a nucleic acid probe or primer which hybridizes to the Plasmodium berghei extra chromosomal genetic element (see sequence alignment provided herewith showing the nucleic acid of Gardner et al to comprise a P. berghei nucleic acid; see page 1067, col. 1, DNA analysis, first paragraph) "oligonucleotide primers" and "PCR amplification" and "primer extension, page 1067, col. 2, paragraph 2"; see page 1068, col. 2, paragraph 1 "probes 32 P-labeled in vitro transcripts complementary to the expected 3' end of the LSU rRNA".)

17. **(c) Detecting** said hybridization resulting from the contacting step (b), wherein the detection agent comprised an nucleic acid that consisted of at least 15 consecutive nucleic acids of SEQ ID No 1, nucleotides 1147-1740, wherein the reference disclosed an agent that shared 100% sequence identity over 117 nucleotides of Applicant's recited range of SEQ ID NO 1.

Instant claims 60-62: wherein the contacting step is performed under low, moderate or high stringency conditions (see Gardner 1993, page 1067, col. 2, DNA analysis, incorporates by reference 7 and 8 , in light of Gardner et al 1991(a) and (b) the analysis conditions, (see Gardner et al 1991, pages 78-79, Materials and Methods; and Gardner et al 1991, page 116, Materials and methods) shows incubation conditions for hybridization reagents to include 5x SSPE at 60 degrees C, at 42 degrees C, 50% formamide 5X SSPE; 3 X 15 minuets 2X SSPE at 65 degrees C; and 80% formamide/0.4 M NaCL heated to 85 degrees C for 5 minutes and overnight at 50 degrees C.)

Instant claim 63-64:wherein detecting comprises identifying a signal produced by a reporter molecule, the signal being an identifiable signal from a radioisotope or a non-isotopic reporter molecule (see Gardner et al 1993, page 1068, Figure 1, "Densitometric analysis" produces a

detectable signal (see figure 1, graph and bands); as well as col. 2, paragraph 1, middle of paragraph "32P-labelled in vitro transcripts complementary to the expected 3' end of the LSU rRNA").

Instant claim 68: wherein the Plasmodium malarial agent of humans is Plasmodium falciparum (see Gardner et al, title, page 1067).: wherein the biological sample comprises blood or nucleic acid extracted from said blood (see Gardner et al, 1993, page 1068, col. 1, "total RNA extracted from parasitized erythrocytes".

The sample of Gardner et al comprised an unknown biological sample portion, specifically the contents and DNA sequence of Plasmodium falciparum 35 kDa circular DNA extra chromosomal genetic element. The biological sample of Gardner was a parasitized erythrocyte sample (see page 1068, col. 1, Transcript analysis, paragraph 5).

The probe or primer was derived from the LSU rRNA (see page 1068, col. 1, paragraph 5 "an oligonucleotide complementary to sequence near the 5' end of the LSU rRNA" and " The complete DNA sequence of the LSU gene is deposited in the EMBL database under the accession number X61660", col. 1, paragraph 4).

The detection was by RNA PCR (see page 1068, col. 1, paragraphs 3-5); specific portions of the LSU rRNA genes were made (see Table 1, page 1070, col.1-2, especially, col. 1, first three lines define the most conserved positions and Table 1, col. 2; Figure 4) that comprises a LSU rRNA nucleic acid sequence of SEQ ID NO 1, nucleotides 1147-1740 that is conserved (complementary to "A/U", see page 1068, col. 1, paragraph 3) and found in an extra chromosomal element circular DNA that is a plastid (see sequence alignment) of a human malarial agent, wherein the probe or primer hybridized to DNA from a human malarial agent in

the sample (see Figure 4, page 1070); to permit detecting hybridization (see page 1070, figure 4), wherein the probe was at least 15 nucleotides in length (see page 1067, materials and methods, DNA analysis section and sequence alignment for X61660 and Figure 4, image and narrative). The hybridization conditions for RNA analysis were disclosed in light of references 7 & 8 (see page 1067, col. 2, paragraph 2, lines 1-2; Gardner et al 1991, Molecular and Biochemical Parasitology, Vol. 48, (reference of record) define a plurality of hybridization conditions, see page 78, col. 2, paragraphs 2-3 and col. 1-2 of page 79, the conditions being low, medium and high stringency conditions). Amendment of the claims to be only a probe or primer that comprises nucleotides 1147 to 1740 of SEQ ID No 1 could obviate this rejection. Gardner et al inherently anticipate the instantly claimed invention.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 65 and 70-71 **are** rejected under 35 U.S.C. 103(a) as being unpatentable over Gardner et al (1993, Nucleic acid research, reference of record, as applied to claims 59-64 and 66-69 above) in view of Obst et al, (1990, Histochemistry, reference of record).

Gardner et al teach and show a method of detecting a human Plasmodium malarial agent in a biological sample, the method comprising the steps of:

contacting a blood derived (erythrocyte) biological sample with a probe or primer (see DNA analysis section, page 1067, col. 2; page 1070, col. 1, first three lines define the most

conserved positions and Table 1, col. 2; Figure 4) that comprises a LSU rRNA nucleic acid sequence of SEQ ID NO 1, nucleotides 1147-1740 that is conserved (complementary to "A/U", see page 1068, col. 1, paragraph 3) and found in an extra chromosomal element circular DNA that is a plastid (see sequence alignment) of a human malarial agent, wherein the probe or primer hybridized to DNA from a human malarial agent in the sample (see Figure 4, page 1070); to permit....

detecting hybridization (see page 1070, figure 4), wherein the probe was at least 15 nucleotides in length (see page 1067, materials and methods, DNA analysis section and sequence alignment for X61660 and Figure 4, image and narrative).

Gardner et al (page 1068, col. 1, paragraph 3, middle of paragraph), teaches a highly conserved sequence of P.falciparum, the complement thereof was incorporated into a primer for detecting a Plasmodial malarial agent of human in a biological sample and the primer comprised a highly conserved sequence for P.berghei (see sequence alignment of X61660), and utilized methods that measured detectable signals, one being non-radioactive and the other being radioactive, but differs from the instantly claimed invention by failing to show the signal to be generated by a non-isotopic reporter molecule biotin, and the biological sample to be a dried blood sample.

Obst et al teach a method of detecting a Plasmodium malarial agent in a biological sample, the method comprising the steps of: contacting and detecting hybridization in a dried blood sample (see page 101, col. 2, material and methods, paragraph 2) which utilized a biotin reporter molecule (see page 102, col. 2, paragraph 3; page 103, col. 1-2 Discussion section and all frames of Figure 1) in an analogous art for the purpose of detecting a malarial agent utilizing

a non-isotopic reporter molecule which generates a specific signal with high resolution (see page 102, col. 2, paragraph 2, last three lines).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of Gardner et al to include the analysis of dried blood samples and a biotin non-isotopic signal reporter molecule as suggested and taught by Obst et al because both Gardner et al and Obst et al teach methods of detecting a malarial agent in a blood derived biological sample, and Obst et al teaches that dried blood smears are readily used as a biological sample for the detection of a malarial agent, and Obst et al also teaches the advantage of utilizing a biotin non-isotopic reporter molecule for the attainment of enhanced signal generation (see page 102, col. 2, hybridization signal as a function of the probe).

In the absence of a showing of unexpected results, the person of ordinary skill in the art would have been motivated by the reasonable expectation of detecting a malarial agent in a dried blood sample utilizing an LSU rRNA biotin report molecule utilizing the probe or primer of Gardner et al with the biotin reporter molecule of Obst et al because Obst et al teach a non-isotopic reporter molecule biotin defined and provided means for generating a specific signal with high resolution (see page 102, col. 1, paragraph 3, signal detection and col. 2, paragraph 2, last three lines) due do the ability of biotin to specifically interact with a fluorescently labeled anti-biotin antibody system which resulted in a highly amplified the biotin signal reporter molecule of high resolution. Gardner et al in view of Obst et al obviates the instantly claimed invention.

Conclusion

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
4/27/05